

REMARKS

Formal Matters

Claims 8 and 10 were examined and stand rejected.

Claims 8 and 10 are pending after entry of the amendments set forth herein.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

Support for the amendments to claims 8 and 10 can be found throughout the specification, at, for example, page 51, line 14 through page 52. As such, no new matter has been added.

Drawings

The handwritten corrections in Figures 1-4, as originally submitted, have been corrected. The corrections reflect matter that was originally filed and thus does not introduce new matter. Entry of the foregoing amendment is respectfully requested.

Claim Objections.

Claim 10 was objected to for depending from a non-elected claim. Applicants have amended the claim so that it no longer depends from the non-elected claim. No new matter has been added by this amendment. Applicants submit that Claim 10 is a properly written independent claim.

Rejection under 35 U.S.C. § 112, 1st paragraph.

Claims 8-10 have been rejected under 35 U.S.C. § 112, 1st paragraph because it is asserted in the Office Action that the specification, "while being enabling for a transgenic mouse whose genome comprises a homozygous disruption in the nucleotide sequence set forth in SEQ ID NO: 1, wherein said mouse exhibits the following phenotypes as compared to a wild-type mouse: a decrease in average velocity of movement during open

field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test, does not reasonably provide enablement for all other transgenic non-human animals.” (Office Action, page 3)

It is recommended in the Office Action that “the claimed invention is properly interpreted with regard to the disclosed phenotype of the exemplified transgenic mice comprising a disruption of the nucleotide sequence set forth in SEQ ID NO: 1.” (Office Action, page 4). Applicants have adopted this recommendation and amended claims 8 and 10 accordingly. As such, Applicants believe that this rejection may be withdrawn.

It is also recommended in the Office Action that “limiting claim 8 to a transgenic mouse whose genome comprises a homozygous disruption of the nucleotide sequence set forth in SEQ ID NO: 1 and claim 10 to an ES cell would be sufficient to overcome this aspect of the rejection.” (Office Action, page 6). Applicants have adopted this recommendation and amended claims 8 and 10 accordingly. As such, Applicants believe that this rejection may be withdrawn.

It is also recommended in the Office Action that “inclusion of a phenotype associated with a disruption of the nucleotide sequence set forth in SEQ ID NO: 1 in a mouse in the claim would overcome this aspect of the rejection.” (Office Action, page 8). Applicants have adopted this recommendation and amended claims 8 and 10 accordingly. As such, Applicants believe that this rejection may be withdrawn.

In light of the foregoing, Applicants submit that the rejections of the above-cited claims under 35 U.S.C. § 112, first paragraph, both as to enablement and/or written description, are overcome in view of the amendments and remarks set forth herein. The Examiner is thus respectfully requested to withdraw these rejections.

Rejection under 35 U.S.C. § 102(a).

Claims 8 and 10 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Stanley et. al. (Genesis, 2000, Vol. 26, page 259-264).

To anticipate a claim, a reference must teach every element of the claim. “A claim is anticipated [under §102] **only if each and every element as set forth in the claim is**

found . . . in a single prior art reference.” MPEP §2131 *citing* (Verdegaal Bros. V. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987))

The Examiner asserts that the Stanley reference discloses the generation of a transgenic mouse with a homozygous disruption in the cerberus gene and that the method for producing the transgenic mouse used a construct comprising a nucleotide sequence homologous to regions of exon 1 of the cerberus gene . . . which was introduced into a mouse embryonic stem cell.” In support of this assertion, the Examiner specifically points to page 260, 1st paragraph under the Results section and page 261-262 of the Stanley reference.

Applicants respectfully point out that the Stanley reference is focused only on LacZ staining to identify perturbation of embryogenesis and postnatal life of homozygous cer1 knockout mice. In particular, the Stanley reference discloses that “mice homozygous for this allele . . . showed no apparent perturbation of embryogenesis or later development.” (Stanley, page 259) As described in applicants’ specification and in this Amendment, the instant invention is directed to a knockout mouse with phenotypic abnormalities such as for example, a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test. The Stanley reference provides no suggestion that such mice would exhibit any such phenotype.

Because the Stanley reference fails to disclose the generation of cerberus gene knockout mice (and the attendant aspects, such as the targeting construct therefor, or methods of making constructs or mice, or cells isolated therefrom) with the above-mentioned phenotypes, Stanley fails to anticipate the claimed invention. As such, Applicants respectfully request that the rejection of pending claims 8 and 10 under 35 U.S.C. § 102(a) as being anticipated by Stanley et al (Genesis, 2000, Vol. 26, page 259-264) be withdrawn.

Rejection under 35 U.S.C. § 103(a).

Claims 8 and 10 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Cappechi et. al. (*Scientific American*, 1994, pp 52-59) in view of Biben et. al. (*Developmental Biology*, 1998, 194, pp 135-151).

In order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference(s) **must teach or suggest all the claim limitations**. See MPEP §2143.

The references, either alone or combined as suggested in the Office Action, fail to teach or suggest that cerberus knockout mice would exhibit phenotypic abnormalities such as for example, a decrease in average velocity of movement during open field testing, a decrease in total distance traveled during open field testing, an increase in the number of fecal boli during open field testing, and a decrease in total time immobile during the tail suspension test.

Accordingly, the references fail to establish a *prima facie* case of obviousness. As such, Applicants submit that the amended claims are not obvious in view of the amendments and remarks set forth above. Accordingly, Applicants respectfully request that the rejection of claims 8 and 10 under 35 U.S.C. § 103 be withdrawn.

Conclusion.

Applicants submit that all of the pending claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1271.

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Respectfully submitted,
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